Intestinal Obstruction Due to Colonic Stricture Following Neonatal Necrotizing Enterocolitis

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After resolution of acute necrotizing enterocolitis (NEC), six of 31 surviving infants (19%) developed late ischemic stricture of the colon. Stricture occurred after both medical and surgical treatment for NEC, and in both functional and defunctionalized bowel. In medically-treated infants, the symptoms of intestinal obstruction usually began six to eight weeks after NEC. Surgically-treated infants developed asymptomatic strictures distal to an enterostomy. Barium enema was the appropriate diagnostic study for both groups. Operative management consisted of segmental colonic resection with frequent use of enterostomy. On histopathologic examination, resected strictures showed a spectrum of the reparative process after intestinal ischemia, ranging from obliterative scar to near-normal colon. Because delayed diagnosis led to the death of one of our infants, we recommend a barium enema for early diagnosis of stricture about six weeks after NEC, whether initial treatment was medical or surgical. In a recent infant, two colonic strictures were thus diagnosed and resected prior to development of symptoms of intestinal obstruction.

ALTHOUGH THE SURVIVAL among infants with necrotizing enterocolitis (NEC) has improved steadily in the past decade,[15] a substantial number of the survivors develop an additional life-threatening surgical problem: intestinal obstruction. With few exceptions, obstruction is secondary to stricture as a consequence of cicatricial healing of a segment of intestine injured by ischemia. In this report, we review our experience in the diagnosis and management of seven infants who required eight operations for colonic stricture following NEC.

Patients and Methods

From January, 1975, through July, 1979, 46 infants with NEC were treated in the Neonatal Intensive Care Unit at the University of New Mexico School of Medicine. According to the classification of Bell, *et al.*[3], 20 infants had Stage II NEC and 26 infants had Stage III NEC. All of the stage II infants were treated medically; all but one of the Stage III infants were operated on.

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Among the 31 surviving infants, six (19%) developed intestinal stricture, four after medical, and two after surgical treatment. The seventh patient in this report was treated by one of the authors at the Children's Hospital of Denver in 1975. There were five boys and two girls. All were Caucasian. Birth weight ranged from 1140 to 3232 g. Gestational age ranged from 30 to 41 weeks.

Acute Episode of NEC

The diagnosis of NEC was established by the clinical triad of abdominal distention, gastrointestinal bleeding, and radiographic evidence of pneumatosis intestinalis.[1] In all but one infant, this syndrome developed during the first week of life. Initial medical treatment consisted of nasogastric suction, intravenous fluids, parenteral antibiotics and, in most cases, an aminoglycoside antibiotic by gavage.[1] Of the seven infants who subsequently developed stricture, four infants recovered from the acute episode of NEC with medical management and three required operation. The operation in these three infants was resection of gangrenous or perforated intestine and either double enterostomy or Mikulicz enterostomy. One operation also included colorraphy for three necrotic yet unperforated foci in the transverse colon, distal to the enterostomy site. No primary anastomoses were performed.

Development of Intestinal Stricture

The seven infants had a total of eight late operations for stricture, five to 14 weeks after acute NEC. Of the four infants who developed stricture after medical management of NEC (Table 1), three had acute intestinal obstruction, manifested by vomiting, abdominal distention, and radiographic findings of dilated

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TABLE 1. *Stricture After Medical Management of Acute NEC*

Case No.	Sex	Birth Weight (g)	Interval After Acute NEC to Operation	Site of Obstruction	Roentgenographic Findings on BE	Pathologic Findings	Surgical Management	Outcome
1	M	1474	14 wk	Sigmoid colon	Complete occlusion	Stricture, severe, with ulcer	Sigmoid resection, primary anastomosis	Died, leak, sepsis 14 d postop
2	M	3232	6 wk	Colon, splenic flexure	Complete occlusion	Stricture, moderate	Colostomy, (resection and anastomosis at 2nd stage operation)	Alive and well
3	M	1140	8 wk	Cecum	No BE-acute obstruction	Stricture, severe	Ileocecal resection, Mikulicz enterostomy	
			10 wk	a) Descending colon and b) Distal limb, enterostomy	a) Partial occlusion and b) Not visualized	a) Stricture, moderate and b) Inflammation and fibrosis	Colon resection, primary anastomosis, revision of enterostomy	Alive and well
4	F	1675	6 wk	a) Transverse colon and b) splenic flexure	Partial occlusion both sites	Strictures, moderate, both sites	Colon resection, primary anastomosis	Alive and well

intestinal loops with multiple air–fluid levels. Onset of these symptoms was gradual in two infants but abrupt in one infant. The fourth infant (Case 4) was asymptomatic and tolerating her feedings well, but stricture was diagnosed by a follow-up barium enema. The three infants who developed stricture after surgical management of acute NEC (Table 2) also were asymptomatic. Their strictures were located in defunctionalized intestine distal to an enterostomy. No stricture occurred in bowel proximal to an enterostomy.

Infants with acute intestinal obstruction were prepared for emergency operation by nasogastric suction, rapid correction of fluid and electrolyte deficits, administration of intravenous antibiotics and a bolus of albumin or blood. Adequate flow of urine (1–2 ml/kg/hour) was established prior to anesthesia. The operation was carried out under general anesthesia, with close monitoring of vital signs, in an operating room heated to 26–29 C.

Infants with strictures not producing acute intestinal

TABLE 2. *Stricture After Surgical Management of Acute NEC*

Case No.	Sex	Birth Weight (g)	Prior Operation for Acute NEC	Interval After Acute NEC to Operation	Site of Obstruction	Roentgenographic Findings on BE	Pathologic Findings	Surgical Management*	Outcome
5	M	2040	Right hemicolectomy, ileostomy†	12 wk	a) Descending colon and b) Sigmoid colon	a) Complete occlusion and b) Partial occlusion	1) Stricture, severe and b) Stricture, moderate	Colon resection, primary anastomosis	Alive and well
6	M	1503	Ileal resection, Mikulicz ileostomy	12 wk	a) Descending colon and b) Distal limb, ileostomy	a) Complete occlusion and b) Not visualized	a) Normal colon (pseudostricture) and b) Inflammation	Colon resection, primary anastomosis, revision of ileostomy	Alive and well
7	F	3232	Colon resection, colostomy, colorraphy	5 wk	Transverse colon	Partial occlusion	Normal colon (pseudostricture)	Colon resection, primary anastomosis	Alive and well

* All three patients had a proximal enterostomy, which was closed at a separate operation 9 days to three weeks later.

† This infant was also operated on for acute intestinal obstruction due to adhesions eight weeks after operation for acute NEC.

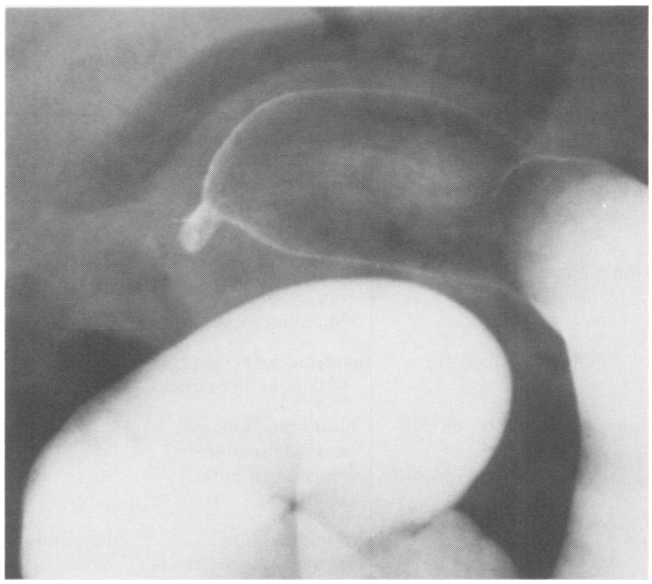

FIG. 1. (Case No. 2) Barium enema showing complete obstruction of the transverse colon near the splenic flexure.

obstruction were operated on electively. Preoperative preparation consisted of administration of several colonic irrigations (20–60 ml of saline) and a clear liquid diet for 12–24 hours. Parenteral antibiotics were begun just prior to operation and continued for 72 hours. Postoperative decompression by nasogastric tube was maintained until the infant resumed passing stools.

Results

Radiographic Findings

Barium enema was carried out in seven of the eight instances of intestinal stricture. One of the infants with acute intestinal obstruction was operated on without a barium enema. In each of the seven barium enemas, one or more strictures, manifested by complete or partial occlusion of the colonic lumen to the flow of barium, was identified. Three infants had a complete occlusion, two infants had a partial occlusion, one infant had two partial occlusions, and one infant had both a complete and a partial occlusion (Figs. 1 and 2). The length of the occluded segment varied from 0.5 to 3 cm. The margins of the stricture were occasionally tapering, but more commonly abrupt. In two infants glucagon was administered in an attempt to distinguish spasm from true intestinal stricture.[11] In both instances the barium enema was unchanged after glucagon. Two strictures were not visualized by barium enema. Both were located in defunctionalized bowel distal to a Mikulicz enterostomy and proximal to a second stricture. Antegrade contrast studies of the defunctionalized segment were not completed in these two infants because attempts to cannulate the distal limb of the Mikulicz enterostomy were unsuccessful.

Operations for Stricture

Three of the four infants who developed stricture after medically-treated NEC required an emergency operation for acute intestinal obstruction (Table 1). The procedures were: resection of a sigmoid stricture and primary anastomosis, colostomy (with subsequent staged resection of a stricture), resection of a cecal stricture and Mikulicz enterostomy. The latter infant (Case 3) required a subsequent operation for a colonic stricture distal to the Mikulicz enterostomy. The fourth medically-treated infant (Case 4) did not have acute intestinal obstruction. She was operated on electively, for two asymptomatic strictures of the transverse colon. Segmental colonic resection and primary anastomosis were performed. All four instances of stricture after surgical treatment for NEC (Cases 3, 5, 6, and 7) occurred in defunctionalized intestine, and were treated by elective operation consisting of colonic resection and primary anastomosis. Two of these anastomoses were by the open technique and two were by the closed technique. Two of the operations also included revision of the Mikulicz enterostomy to remove a stricture of the distal limb. These four infants (Cases 3, 5, 6, and 7) underwent enterostomy closure at a separate operation nine days to three weeks later.

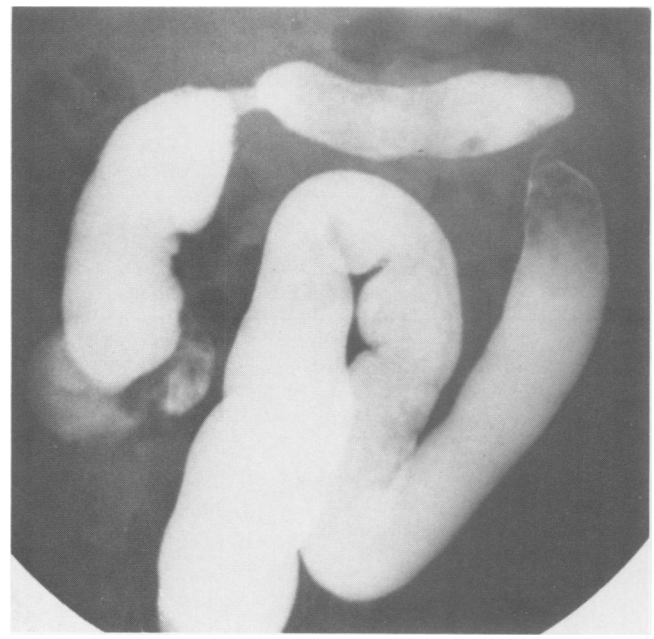

FIG. 2. (Case NO. 4) Barium enema demonstrating two sites of narrowing in the colon, one at the splenic flexure, and one in the right transverse colon. These areas of narrowing did not change after administration of parenteral glucagon, indicating that they represented fixed strictures rather than spasm. At the time of this examination, the patient had not manifested symptoms of intestinal obstruction.

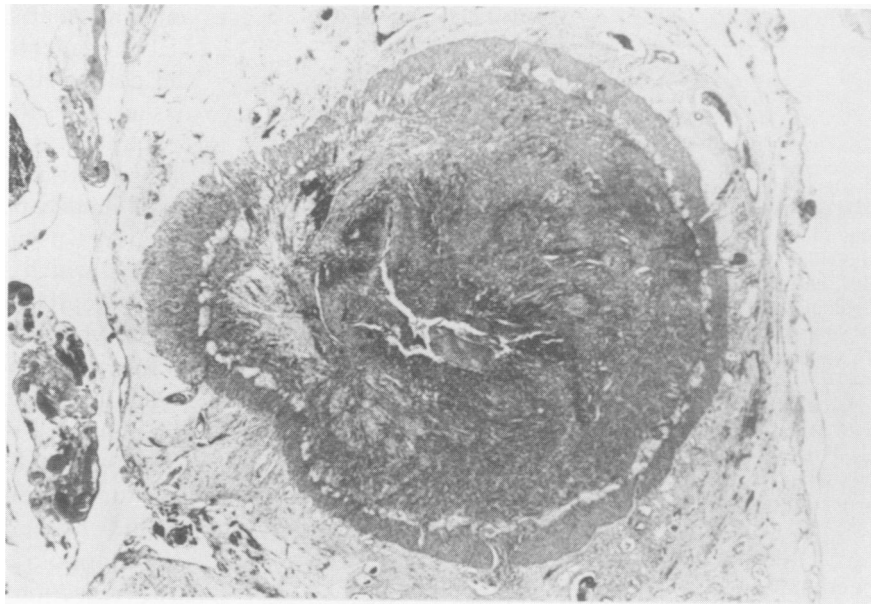

FIG. 3. Severe stricture (Case No. 3). Extensive fibrous tissue replacement of mucosa and submucosa with fibrosis of some portions of the muscular wall.

Pathologic Findings

Because four infants had multiple strictures, pathologic sections of a total of 12 strictures were available for study. Eleven of the 12 strictures contained gross abnormalities consisting of thickening in ten specimens and ectasia in one. The twelfth specimen (Case 6) consisted of a resected segment of colon which appeared grossly normal. Microscopically, ischemic strictures were graded as severe or moderate. Severe strictures were characterized by replacement of the submucosa and muscularis by granulation tissue and fibrosis, producing obliteration of the lumen (Fig. 3). Moderate strictures had intact mucosa and muscularis, with a lesser degree of submucosal granulation and fibrosis, producing luminal narrowing (Fig. 4). There were three severe strictures and five moderate strictures. An ulcer was superimposed on one of the severe strictures. Two additional inflammatory strictures occurred at the distal limb of Mikulicz enterostomies. The term pseudostricture was applied to the two remaining specimens in which the microscopic appearance of the colon was normal or near-normal.

Clinical Results

There was one death. This was the infant (Case 1) in whom the diagnosis of stricture was delayed until 14 weeks after NEC, when acute colonic obstruction occurred. (In retrospect, the diagnosis could have

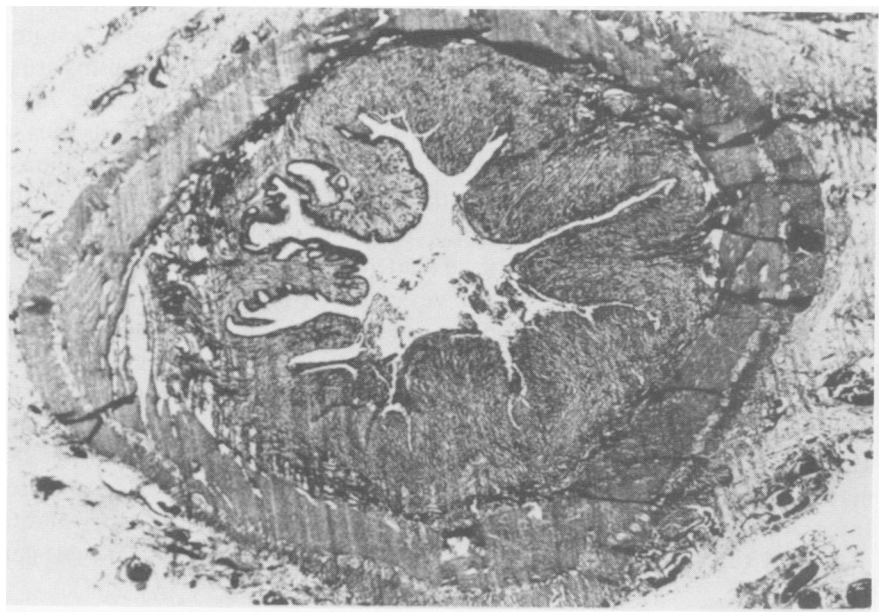

FIG. 4. Moderate stricture (Case No. 4). Granulation and fibrous tissue replace the submucosa and mucosa with partial luminal surface re-epithelialization. The muscular wall is uninvolved.

TABLE 3. *Incidence of Stricture Following NEC*

Authors	No. of Patients	No. of Survivors	No. of Strictures (% in Survivors)
Kosloske and Martin (1973)[7]	22	16	3 (19%)
Reid and Shannon (1973)[16]	10	9	4 (44%)
Santulli, et al. (1975)[17]	64	14	3 (22%)
O'Neill, et al. (1975)[13]	52	34	1 (3%)
Bell, et al. (1976)[2]	56	42	8 (19%)
Touloukian (1976)[18]	20	9	2 (22%)
O'Neill and Holcomb (1979)[14]	33	20	2 (10%)
This series	46	31	6 (19%)

Each series includes both medically and surgically-treated infants with acute NEC, except Reid and Shannon[16] (all medical—no surgical treatment was used for acute NEC) and O'Neill and Holcomb[14] (all surgical—medically-treated infants were not included in this series).

been made on a barium enema obtained ten weeks after NEC.) This infant, the first in our series (1975), underwent resection and primary anastomosis. Postoperatively he developed massive gastrointestinal hemorrhage from a stress ulcer, and ultimately died of sepsis following a leak from the colonic anastomosis. One infant (Case 2) developed postoperative complications. His colostomy retracted, leading to recurrent intestinal obstruction and sepsis. Revision of the colostomy corrected these problems. Three of the seven infants required central venous lines for total parenteral nutrition. The six surviving infants are well at follow-ups ranging from eight months to four years.

Discussion

Our incidence of stricture among 19% of infants surviving acute NEC is similar to the incidence reported in several earlier series (Table 3). The considerable range in incidence from 3 to 44% in various series probably reflects case selection, different criteria for medical or surgical treatment, and changing survival rates. The original report of colonic stricture after NEC was by Krasna, et al.[9] in 1970.

The pathogenesis of intestinal stricture following NEC, akin to that following ischemic colitis in adults, is the reparative process following an acute decrease in flow through the intramural blood vessels.[4,12] In the classic description by Marston, et al.,[10] ischemic injury of the colon may take one of three courses. If the full thickness of the colonic wall is infarcted, transmural gangrene results. If the mucosa alone is infarcted, bleeding and ulceration occur, but the mucosa may heal completely and regain normal function. Intermediate between these two extremes is infarction of partial thickness of the colonic wall. The mucosa and muscularis mucosae are destroyed, but enough viable elements remain to prevent complete death of the colon. Healing is by proliferation of granulation tissue and subsequent fibrosis, resulting in stricture formation. Our infants demonstrated a spectrum of colonic stricture, ranging from obliterative scar to histologically normal colon (pseudostricture). We have discussed pseudostricture of the colon in a previous report[8] which includes Cases 6 and 7. We believe that it represents an ischemically-injured segment of colon which has healed histologically but continues to function abnormally, and thus should be resected.

The operation for stricture consists of resecton of the abnormal segment, with generous margins. If the infant is acutely ill from intestinal obstruction, primary anastomosis should be avoided and the bowel ends should be exteriorized. Alternatively, in such infants, a diverting colostomy or enterostomy may be performed, with resection of the stricture at a later operation. Our single death occurred in the first patient of this series, a sickly infant with acute colonic obstruction who died from a leaking primary anastomosis. We have since reversed primary anastomosis for healthy infants undergoing elective surgery. Sick infants are managed by staged operations, including an enterostomy. Details of operative techniques for NEC were described in an earlier report.[6]

In all surgically-treated survivors of NEC, it is mandatory to obtain a barium enema prior to enterostomy closure, to rule out stricture. Usually this is carried out six to 12 weeks after the acute episode of NEC, when the infant is in a good nutritional state. Strictures found in the defunctionalized bowel are managed by resection and primary end-to-end anastomosis. The open technique may be superior for the anastomosis; experimental evidence suggests that closed anastomosis in defunctionalized colon may lead to septum formation and reobstruction.[5] Multiple short strictures may be treated by Heinecke-Mikulicz enteroplasties to avoid sacrifice of substantial lengths of good colon between them. The enterostomy may be closed at the same operation, although we prefer to close it at a separate procedure two to four weeks later.

Intestinal stricture following NEC carries a consequential mortality and morbidity. In Bell's collected series of 27 infants with strictures after NEC, there were five deaths.[2] The mortality is chiefly due to aspiration pneumonia and to septic complications in the early postoperative period. Several deaths have been associated with delayed diagnosis and treatment.[2,9] Infants developing stricture tend to display poor weight gain, abdominal distention, and vomiting.

The risk of death or complication may be decreased by earlier diagnosis and operation even prior to the onset of obstructive symptoms.

Because of our 19% incidence of colonic stricture after NEC, we believe that a barium enema is indicated in all medically-treated survivors of NEC at about six weeks after the acute episode, even in the absence of symptoms of intestinal obstruction. In our most recently treated infant (Case 4, from 1979) two colonic strictures (Fig. 4) were diagnosed by such a barium enema (Fig. 2) before any obstructive symptoms had developed. Elective colonic resection with primary anastomosis was successfully performed. Had we waited to study her until she became clinically obstructed, a two-stage procedure would probably have been necessary, at an increased operative risk. We do not recommend routine barium contrast studies of the small intestine in asymptomatic infants, since the small intestine is a rare ischemic stricture after NEC. Intestinal obstruction due to adhesions, which we encountered only once during the four and one-half years of this study, also appears to be rare following NEC.

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